The Effect of Sequential Contrast Agent Studies on the Assessment of Relative Cerebral Blood Volume

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INTRODUCTION. Dynamic MR imaging of the first-pass of a susceptibility contrast agent confined to the intravascular space has enabled the creation of relative cerebral blood volume (rCBV) maps. This approach has been used for the evaluation of brain neoplasms [1] and for the detection of brain activation changes [2]. Comparison of rCBV for cortical gray versus periventricular white matter yielded a ratio of two, a value that has been well documented in the literature, thus supporting the accuracy of this approach [3]. Recently though, the stability and reproducibility of this method for sequential rCBV measurements has been called into question with results indicating artifactually elevated estimates of rCBV with subsequent contrast agent doses [4]. This has important implications for the utility of susceptibility-rCBV methods to evaluate *changes* in blood volume that might occur between resting and activated states. However, the results described in [4], were derived using a whole brain region of interest (ROI). Whether the ratio of gray to white matter rCBV remained constant with subsequent contrast agent doses was not addressed, and was the primary goal of the current study.

METHODS. To study the effect of multiple doses of contrast agent, two normal subjects were studied with three sequential boluses of Gd. All images were obtained using a Bruker BIOSPEC 3T imaging system. Interleaved gradient echo (64×64, TR=1s, TE=27.2 ms) and spin echo images (64×64, TR=1s, TE=110 ms) were acquired in the axial plane at, 7 mm thick slices, over 180 seconds. Sixty seconds into the acquisition, 0.05 mmol/kg Gd-DTPA, i.e. Prohance® was bolus (approx. 6-8s) injected through a 12-gauge venous catheter. From 1-12 mins later, a second injection was given, followed by a third after the same time interval, both 0.05 mmol/kg.

The rCBV for each pixel was computed according to the following relationship:

$$rCBV \propto \frac{-1}{TE}\int \ln\frac{S(t)}{S(0)} \qquad (1)$$

where $S(t)$ is the MR signal intensity, $S(0)$ is the averaged baseline signal intensity, and TE is the echo-time. The initial point for the integration was determined on the basis of a gamma-variate fit to the concentration-time image data. The gamma-variate function with a recirculation cut-off is defined as follows:

$$S(t) = Q(t-t_0)^r e^{-(t-t_0)/b} \qquad (2)$$

where $S(t)$ is the MR signal intensity, Q, r,b are fit constants, t is the injection time, and t_0 is the appearance time of the tracer. Integration limits were set from t_0 to (t_0+12) points. For the whole brain CBV a ROI of 25×25 voxels was used and histogram analysis was carried, to assess the CBV distribution on a voxel-wise basis. Finally, for the gray/white ratio study, ROIs were selected in cortical gray and periventricular white matter from high-resolution anatomical images.

RESULTS. For the range of doses studied, we observed changes in the whole brain CBV as a function of contrast agent dose (Table 1.), similar to previous studies using whole brain [4]. However, a histogram analysis of the gradient and spin echo rCBVs (Fig. 1, Fig. 2) revealed that the relative distribution of blood-volume as a function of contrast agent dose, remains unchanged on a voxel-wise basis, for both gradient and spin echo sequences. Finally, single factor ANOVA reveals that the gray/white matter ratios are not significantly different from dose to dose (Fig. 3).

Table 1.

Sequence	Dose	Subject 1		Subject 2	
		rCBV	ΔrCBV	rCBV	ΔrCBV
GE	*1*	7399	-	4628	-
	2	6200	-16.2%	11559	-150.6%
	3	6752	8.90%	11935	3.25%
SE	*1*	5729	-	1265	-
	2	4237	-26.0%	2740	116.6%
	3	5814	37.2%	4323	57.8%

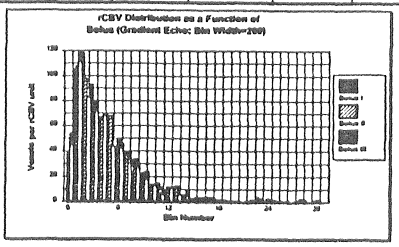
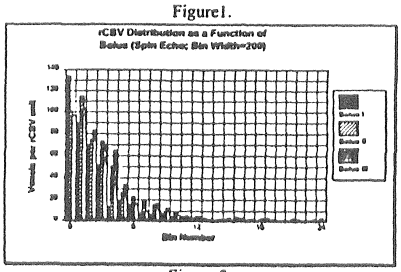


Figure1.



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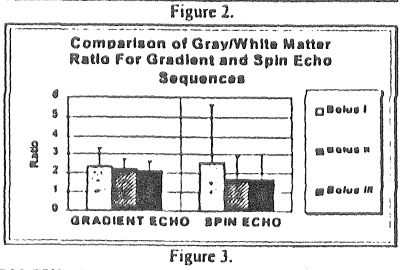

Figure 3.

DISCUSSION/CONCLUSION. This study demonstrates that the utility of sequential contrast agent studies is not limited to computing the rCBV only *after* attaining a relative steady state after multiple boluses [4]. We have demonstrated that the resting blood volume ratio of gray to white matter stays constant from bolus to bolus, enabling us to evaluate *changes* in gray matter rCBV when normalized to white matter rCBV. Such might occur between resting and activated states during brain activation studies. However, this is still not an appropriate method for detecting rCBV changes when both, gray and white matter rCBV are increased, as in the case of hypercapnia studies.

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1998 Abstract Form for Scientific Presentations
INTERNATIONAL SOCIETY FOR
MAGNETIC RESONANCE IN MEDICINE
SIXTH SCIENTIFIC MEETING
SYDNEY AUSTRALIA
APRIL 18-24, 1998

ABSTRACT DEADLINE:
Received no later than NOVEMBER 18, 1997.
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